

Exhibit A

AAW87995
ID AAW87995 standard; protein; 609 AA.
XX
AC
XX
DT 15-APR-1999 (first entry)
XX
DE An alternatively spliced human MCG7 protein.
XX
KW MCG4 protein; gene regulatory function; heat shock protein;
guanine nucleotide exchange factor protein; MCG7 protein;
heat shock-binding protein; MCG18 protein; zinc finger protein; cancer.
XX
OS Homo sapiens.
XX
PN WO853001;A1.
XX
PD 26-NOV-1998.
XX
PF 22-MAY-1998; 98AU-0000380.
XX
PR 23-MAY-1997; 97AU-00006973.
PR 23-MAY-1997; 97AU-00006974.
PR 22-JAN-1998; 98AU-00001458.
PR 22-JAN-1998; 98AU-00001459.
PR 22-JAN-1998; 98AU-00001460.

PA

XX

PI

XX

WPI

XX

DR

N-PSDB

XX

PT

XX

PT

XX

PS

XX

Claim 5; Fig 13b; 80pp; English.

XX

CC

Db 241 NTIMAVUGGLSHSISLKRKETSHVSPTEIKWGLTVEGLTATGNYGRRLAACVFR 300
 QY 301 FPLIGVHKLQDVALQALPDWIDPARTLNGAKMKQKPLSILERAMVTSRPPVQANDL 360
 Db 301 FPLIGVHKLQDVALQALPDWIDPARTLNGAKMKQKPLSILERAMVTSRPPVQANDL 360
 QY 361 LSILTVSLDQYQTEDELQLSLOREPRKSSTSPTSCPTPPRPPVLEWTSAAKPKDQ 420
 Db 361 LSILTVSLDQYQTEDELQLSLOREPRKSSTSPTSCPTPPRPPVLEWTSAAKPKDQ 420
 QY 421 ALVYEHETKMEVESVERAEDVQDGHSQEBEFOIRGNNPPLSARGLDQDGCISREM 480
 Db 421 ALVYEHETKMEVESVERAEDVQDGHSQEBEFOIRGNNPPLSARGLDQDGCISREM 480
 QY 481 VSFLRASSVGLGGRMGMFVNQFNSLSLRPVACRCKALLGTYQGKJCRAGVNCNHCQC 540
 Db 481 VSFLRASSVGLGGRMGMFVNQFNSLSLRPVACRCKALLGTYQGKJCRAGVNCNHCQC 540
 QY 541 KDRLSVERRAOSVSLGSPSPMESHHRASFSLPGRGRSRPAPLPLABIRE 600
 Db 541 KDRLSVERRAOSVSLGSPSPMESHHRASFSLPGRGRSRPAPLPLABIRE 600
 QY 601 EKVQTEGDIVDHL 615
 Db 601 EKVQTEGDIVDHL 615
 QY 595 EKVQTEGDIVDHL 609
 Db 595 EKVQTEGDIVDHL 609

RESULT 3

AAV70961

XX AAV70961 standard; protein; 609 AA.

AC AAV70961;

XX

DT 09-AUG-2000 (first entry)

XX Human Ras signalling pathway associated protein CalDAG-GEFT.

XX Human; Ras signalling pathway; CalDAG-GEFT; calcium; DAG; diacylglycerol;

KW GEF; guanine nucleotide exchange factor; Rapi/RA; diagnosis; treatment;

KW CalDAG-GEFT-associated disorder; drug; transgenic animal model;

KW Ras-associated cancer; protein therapy.

XX Homo sapiens.

OS Homo sapiens.

XX

FT Key Region 150..173

FT Location/Qualifiers /label= SCR1

FT /note= "Structurally conserved region which is highly homologous to Ras superfamily GEFs"

FT Region 220..262

FT /label= SCR2

FT /note= "Structurally conserved region which is highly homologous to Ras superfamily GEFs"

FT Region 299..320

FT /label= SCR3

FT /note= "Structurally conserved region which is highly homologous to Ras superfamily GEFs"

FT Binding-site 433..452

FT /label= PF-hand

FT /note= "calcium binding motif"

FT Binding-site 499..548

FT /label= DAG/phorbol ester-binding domain

FT /note= "present in most protein kinase C family members"

PN W020024768-A2.

XX

PD 04-MAY-2000.

PP 22-OCT-1999;

PR 23-OCT-1998;

PR 16-NOV-1998;

PR 98US-0105507P.

PR 98US-0108685P.

XX (MAST) MASSACHUSETTS INST TECHNOLOGY.

XX PA

XX PI

XX Kawasaki H, Graybiel A, Housman D;

XX DR

XX WPI: 2000-350590/30.

XX N-PSDB; ADD0311.

XX PT

XX Isolated nucleic acid comprises nucleotide sequence encoding protein selected from normal or mutant CalDAG-guanine nucleotide exchange factor.

XX

XX PG

XX Claim 64; Page 90-92; 128pp; English.

XX CC

XX The present sequence is a CalDAG-guanine nucleotide exchange factor (GEFT) from a human frontal cortex and U937 lymphoma cell libraries. The CalDAG-GEFT has substrate specificity for RapiA, dual binding domains for calcium and diacylglycerol (DAG) and highly expressed in brain, particularly in brain ganglia pathways and their axon-terminal regions. Expression of CalDAG-GEFT activates RapiA and inhibits Ras-dependent activation of the extracellular-signal-regulated kinase/mitogen activated protein (ERK/MAP) kinase cascade in 293T cells. The CalDAG-GEFT proteins play an important role in determining the relative activation of Ras and Rapi signalling induced by calcium and DAG mobilisation in brain and hematopoietic organs. The present sequence is used for diagnosis and treatment (by protein therapy) of CalDAG-GEFT-associated disorders. It is also useful for developing drugs and producing cell-lines or transgenic animal models for Ras-associated cancers

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XX Sequence 609 AA;

XX

Query Match 98.6%; Score 3190; DB 3; Length 609;

Matches 608; Conservative 1; Mismatches 0; Indels 6; Gaps 1;

Db 1 MAGTIDLDGKCTVEELLGICIEARTDSKVRDPOLVRLFIMMHWYIISOLAKLHTY 60

Db 1 MAGTIDLDGKCTVEELLGICIEARTDSKVRDPOLVRLFIMMHWYIISOLAKLHTY 60

Db 61 QOSRKDNNSLSLQVKTCHVRWTSAPFDPDMLAOKELKALLQKORGRRHSSID 120

Db 61 QOSRKDNNSLSLQVKTCHVRWTSAPFDPDMLAOKELKALLQKORGRRHSSID 120

Db 121 IDSPVTKWQKQTVQTPNPLSNSQVQWQVQMLISLFDHLPMLAEHLTYLVEASFCKLIFQDAYS 180

Db 121 IDSPVTKWQKQTVQTPNPLSNSQVQWQVQMLISLFDHLPMLAEHLTYLVEASFCKLIFQDAYS 180

Db 181 FVTRGCTVNPFLERFISLPSNSQVQWQVQMLISLFDHLPMLAEHLTYLVEASFCKLIFQDAYS 240

Db 181 FVTRGCTVNPFLERFISLPSNSQVQWQVQMLISLFDHLPMLAEHLTYLVEASFCKLIFQDAYS 240

Db 241 NTIMAVUGGLSHSISLKRKETSHVSPTEIKWGLTVEGLTATGNYGRRLAACVFR 300

Db 241 NTIMAVUGGLSHSISLKRKETSHVSPTEIKWGLTVEGLTATGNYGRRLAACVFR 300

Db 301 FPLIGVHKLQDVALQALPDWIDPARTLNGAKMKQKPLSILERAMVTSRPPVQANDL 360

Db 301 FPLIGVHKLQDVALQALPDWIDPARTLNGAKMKQKPLSILERAMVTSRPPVQANDL 360

Db 361 LSILTVSLDQYQTEDELQLSLOREPRKSSTSPTSCPTPPRPPVLEWTSAAKPKDQ 420

Db 361 LSILTVSLDQYQTEDELQLSLOREPRKSSTSPTSCPTPPRPPVLEWTSAAKPKDQ 420

Db 421 ALVYEHETKMEVESVERAEDVQDGHSQEBEFOIRGNNPPLSARGLDQDGCISREM 480

Db 421 ALVYEHETKMEVESVERAEDVQDGHSQEBEFOIRGNNPPLSARGLDQDGCISREM 480

Db 481 VSFLRASSVGLGGRMGMFVNQFNSLSLRPVACRCKALLGTYQGKJCRAGVNCNHCQC 540

Db 481 VSFLRASSVGLGGRMGMFVNQFNSLSLRPVACRCKALLGTYQGKJCRAGVNCNHCQC 540

Db 541 KDRLSVERRAOSVSLGSPSPMESHHRASFSLPGRGRSRPAPLPLABIRE 600

Db 541 KDRLSVERRAOSVSLGSPSPMESHHRASFSLPGRGRSRPAPLPLABIRE 600

Db 541 KDRLSVERRAOSVSLGSPSPMESHHRASFSLPGRGRSRPAPLPLABIRE 600